Surgical Closure of Atrial Septal Defect Before or After the Age of 25 Years. Comparison with the Natural History of Unoperated Patients

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Introduction. Surgical closure of an atrial septal defect (ASD) before the age of 25 years has been demonstrated to reduce complications during adulthood. However, the outcome for patients operated after the age of 25 is still debated.

Methods. In a retrospective study we examined the outcome of early and late surgical repair of ASD in adults, as compared with the natural evolution of unoperated patients. The study population was 280 patients (mean age 40 ± 18 years) with non-restrictive ASD: 102 patients (group 1) underwent surgery before the age of 25 years, 90 patients (group 2) underwent surgery after the age of 25 years, and 88 unoperated patients were older than 25 years at the time of study (group 3). The variables analyzed were left ventricular systolic function, left atrial dimensions, systolic pulmonary pressure, right ventricular dimensions, the degree of mitral and tricuspid regurgitation, and the prevalence of late atrial fibrillation.

Results. Left ventricular systolic function and the degree of mitral regurgitation were not statistically different between groups. Compared with the patients in group 2, the patients in group 1 had a significantly lower systolic pulmonary arterial pressure ($p < 0.001$) and less dilated right ventricle ($p < 0.001$) and left atrium ($p < 0.001$). The degree of tricuspid regurgitation ($p < 0.001$) and prevalence of atrial fibrillation ($p < 0.001$) were significantly higher in the patients of group 2. Compared with group 3, the patients in group 2 had a significantly lower systolic pulmonary arterial pressure ($p < 0.001$) and less dilated right ventricle ($p < 0.001$). However, the left atrial dimensions, degree of tricuspid regurgitation, and prevalence of atrial fibrillation did not differ in a statistically significant way between the two groups.

Conclusions. Surgical repair of an atrial septal defect in patients over 25 years of age does not fully prevent hemodynamic deterioration and the development of atrial arrhythmias. Therefore it seems that the surgical closure of ASD before adulthood should be strongly recommended.

Key words: *Congenital heart disease. Atrial septal defect. Surgery. Echocardiography. Atrial fibrillation.*

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Cierre quirúrgico de la comunicación interauricular antes o después de los 25 años de edad. Comparación con la evolución natural en pacientes no operados

Introducción. El cierre quirúrgico de la comunicación interauricular (CIA) antes de los 25 años de edad disminuye las complicaciones durante la vida adulta, pero las consecuencias de la intervención en pacientes mayores de 25 años siguen siendo motivo de controversia.

Métodos. Para comparar los efectos de la cirugía precoz y/o tardía con la evolución natural se ha estudiado, de forma retrospectiva, a 280 adultos (edad media 40 ± 18 años) con CIA no restrictiva. Ciento dos pacientes (grupo 1) habían sido operados antes de los 25 años, 90 (grupo 2) habían sido operados después de los 25 años y 88 (grupo 3) no habían sido operados previamente. Se comparó la presión pulmonar sistólica, el tamaño del ventrículo derecho y la aurícula izquierda, el grado de insuficiencia mitral y tricúspide, la función sistólica del ventrículo izquierdo y la prevalencia de fibrilación auricular.

Resultados. No había diferencia en la función sistólica del ventrículo izquierdo o en el grado de insuficiencia mitral entre los tres grupos. Comparado con el grupo 2, el grupo 1 tenía menores presión sistólica pulmonar ($p < 0,001$), tamaño del ventrículo derecho ($p < 0,001$), grado de insuficiencia tricúspide ($p < 0,001$), tamaño de aurícula izquierda ($p < 0,001$) y prevalencia de fibrilación auricular ($p < 0,001$). Comparado con el grupo 3, el grupo 2 presentaba menores presión sistólica pulmonar ($p < 0,001$) y tamaño del ventrículo derecho ($p < 0,001$), pero no existía diferencia en el grado de insuficiencia tricúspide, el tamaño de la aurícula izquierda o la prevalencia de fibrilación auricular.

Conclusiones. El cierre quirúrgico de la CIA después de los 25 años no previene el deterioro hemodinámico o el desarrollo de arritmias auriculares, por lo que se debería concentrar esfuerzos en corregir el defecto antes de la edad adulta.

Palabras clave: *Cardiopatías congénitas. Comunicación interauricular. Cirugía. Ecocardiografía. Fibrilación auricular.*

ABBREVIATIONS

ASD: atrial septal defect.
AF: atrial fibrillation.
SD: standard deviation.
ECG: electrocardiogram.

INTRODUCTION

Surgical repair of *ostium secundum* or venous sinus atrial septal defect (ASD) performed before the age of 25 years could be considered effective surgery without significant residual lesions.[1,2] The closure of an ASD in an adult, even when there is a significant left to right short circuit, may be less than satisfactory. All studies agree that surgery is the most effective medical treatment for patients with serious symptoms, but the data is not conclusive for patients who are less symptomatic.[3-7] When the intervention is performed before the age of 25 years, the size and function of the right ventricle normalize, pulmonary hypertension regresses, there is no evidence of left ventricular dysfunction or dilatation of the left atrium, and the incidence of tricuspid insufficiency and atrial arrhythmias remains low. Nevertheless, the hemodynamic and electrophysiological course of patients who undergo surgery as adults has not been well established.[8-13] The aim of this study is to evaluate the size of the right ventricle, pulmonary pressure, the level of mitral and tricuspid insufficiency, the systolic function of the left ventricle, the size of the left atrium, and the prevalence of atrial fibrillation (AF) in patients with ASD who underwent surgery after the age of 25 years compared toh patients who had surgery before the age of 25 years and to patients older than 25 years of age who did not undergo intervention for the ASD.

METHODS

Study population

We retrospectively analyzed all patients ≥15 years of age with a diagnosis of ASDs followed by the Adult Congenital Heart Disease Unit in our institution between January, 1990 and December, 1999. We excluded from our analysis all patients who presented with the following conditions: *a)* a small ASD with the diameter of the defect being <15 mm and a ratio of pulmonary flow to systemic flow ≤1.5; *b)* age of less than 25 years without previous surgery for ASD, and *c)* other associated congenital malformations, particularly pulmonary stenosis, Ebstein´s anomaly of the tricuspid valve, or non-restrictive ASD. We did not exclude patients with mitral valve anomalies associated with *ostium primum* or *ostium secundum* ASD. We only included those patients who had undergone at least clinical evaluation, a 12-lead ECG study, and a Doppler echocardiograph performed in our center.

The patients were divided into 3 groups. Group l included all patients who had undergone surgery for ASD before the age of 25 years and with at least 1 year of postoperative follow-up. Group 2 included all patients who underwent surgery for ASD after the age of 25 years and with at least 1 year of postoperative follow-up. Group 3 contained all patients older than 25 years of age who had not undergone surgery before their last clinical evaluation and echocardiography study.

Echocardiography evaluation

The echocardiography studies were performed with a Sonos 1000, 2500, or 5500 machine (Philips, Andover, Massachusetts, USA). The size of the left atrium was determined, as was the diastolic dimension of the right ventricle and shortening fraction of the left ventricle using the M technique from the high parasternal position. In all cases the existence of mitral or tricuspid insufficiency was determined by color Doppler and the severity of regurgitation was determined according to previously established criteria.[14-16] For all patients with tricuspid insufficiency, we calculated the systolic pulmonary pressure using the simplified Bernouille equation.[17] For patients in groups 2 and 3 we determined the ratio of pulmonary flow to systemic flow and the diameter of the defect according to previously established methods.[18,19] As the majority of patients in group 1 had undergone surgery before being admitted to our unit, we did not have pre-operative data on these patients available in our database.

Cardiac rhythm

Cardiac rhythm was determined by 12-lead baseline ECG. We considered the AF to be chronic when the baseline ECG, performed during the last clinical evaluation in the clinic, showed AF. Those patients with a history of paroxysmal AF, who were undergoing effective anti-arrythmia treatment, or who had unsustained episodes of atrial arrhythmias on Holter monitoring were considered to be in sinus rhythm.

Statistical analysis

Quantitative variables were expressed as mean ±standard deviation (SD). Distribution by sex, anatomical type of defect, and cardiac rhythm were expressed in percentages. The degree of mitral and tricuspid insufficiency was determined semi quantitatively according to 3 grades (0=absent; 1=slight; 2=moderate,

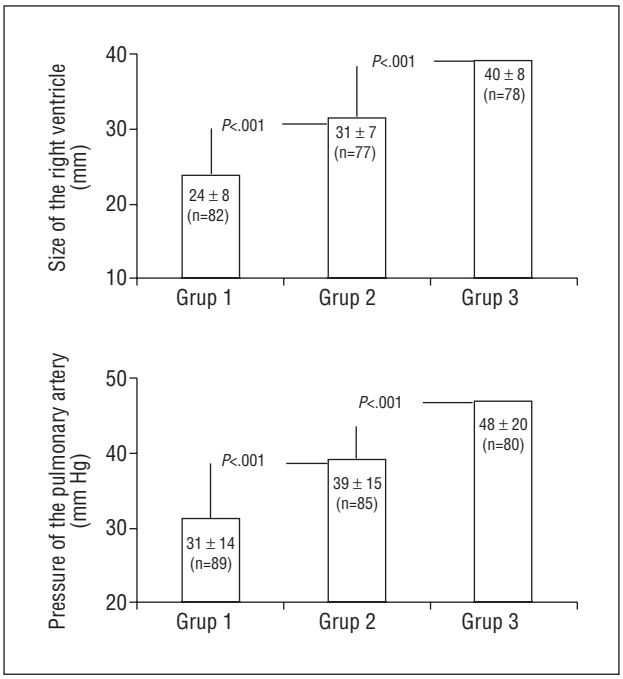

Fig. 1. Comparison of the size of the right ventricle and the systolic pressure of the pulmonary artery among patients with ASD who underwent surgery before the age of 25 years (group 1), after the age of 25 years (group 2), and patients of more than 25 years of age who did not undergo surgery (group 3). Values are presented as mean±standard deviation (SD); n indicates number of cases on which each estimate is based.

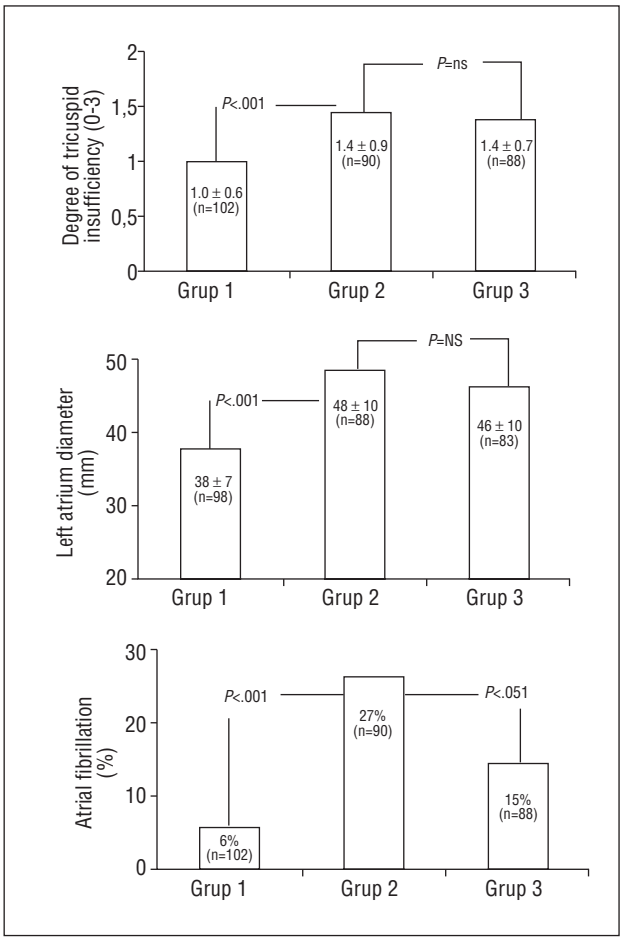

Fig. 2. Comparison of the degree of tricuspid insufficiency, size of the left atrium, and the prevalence of chronic atrial fibrillation among patients with ASD who underwent surgery before the age of 25 years (group 1), after the age of 25 years (group 2), and patients of more than 25 years of age who did not undergo surgery (group 3). Values are presented as mean±standard deviation (SD); n indicates number of cases on which each estimate is based.

and 3=serious) and was also expressed as mean±SD. The results from group 2 were compared with those from group 1 and group 3. Analysis was carried out by the Mann-Whitney U test or the χ^2 test where appropriate. All statistical studies were performed with the SPSS 9.0 statistical program for Windows (SPSS Inc., Chicago, Illinois, USA). In all cases the results were considered statistically significantly when $P<.05$.

RESULTS

Two hundred and eighty patients who met the inclusion criteria made up the population for this study. Mean age was 40 years±18 years, with a range of 15 to 86 years of age. There were 183 women (65%) and 97 men (35%) in the study group. At the time of clinical evaluation, there was a sinus cardiac rhythm in 237 patients (85%) and atrial fibrillation in 43 patients (15%). In 192 patients surgical closure of the ASD had been performed at least 1 year prior to the last clinical evaluation and echocardiography study. The intervention had been carried out before the age of 25 years in 102 cases (group 1) and after the age of 25 years in 90 cases (group 2). The remaining 88 patients had not undergone surgery at the time of the last clinical evaluation and echocardiography study (group 3).

Comparison of patients who underwent surgery before and after the age of 25 years

Table 1 compares the variables analyzed for patients in groups 1 and 2. The patients in group 1 had a significantly lower mean age (22 years±7 years vs 52 years±13 years; *P*<.001), a higher percentage of *ostium primum* ASD (34% vs 9%; *P*<.001), and a longer period of postoperative follow-up (11 years±8 years versus 6.6 years±6 years; *P*<.001). The shortening fraction of the left ventricle and the degree of mitral insufficiency were not significantly different for both groups. Nevertheless, the patients in group 1 had a smaller diastolic size of the right ventricle (23.9 mm±8 mm vs 31.4 mm±7 mm; *P*<.001), less systolic pressure in the pulmonary artery (30.9 mm Hg±14 mm Hg vs 38.9 mmHg±15 mm Hg; *P*=.001), a lower degree of tricuspid insufficiency (1.0±0.7 vs 1.45±0.9; *P*<.001), smaller left ventricle (37.8 mm±7 mm vs 48.3 mm±10 mm;

P<.001), and a lower prevalence rate of atrial fibrillation (6% vs 27%; *P*<.001) (Figures 1 and 2).

Anatomical type of ASD

The anatomical type of ASD was *ostium secundum* in 197 cases (70% of patients), *ostium primum* in 52 cases (19% of patients), and venous sinus in 31 cases (11% of patients). There were 35 patients with *ostium primum* ASD in group 1 (34% of patients), 8 patients in group 2 (9% of patients), and 9 patients in group 3 (10% of patients). The patients with *ostium primum* ASD who underwent surgery were younger (*P*<.001), had been operated on at an earlier age (*P*<.001), and had a higher degree of post-operative mitral insufficiency (*P*<.001), but there were no significant differences in systolic pulmonary pressure, the diastolic size of the right ventricle, the degree of tricuspid insufficiency, the size of the left atrium, the left ventricle shortening fraction, or the prevalence of atrial fibrillation (Table 2). When the patients with *ostium primum* ASD were excluded from the general data analysis, the same variables had statistical significance for the total group (Table 3).

Comparison of patients who underwent surgery after the age of 25 years and adult patients who did not undergo surgery

Tables 1 and 3 also show the comparison of the various variables analyzed for groups 2 and 3. The patients in both groups were not different with regard to age, sex, anatomical type of defect, the ratio of pulmonary flow to systemic flow, size of the defect, left ventricle shortening fraction, or degree of mitral insufficiency. Figure 1 shows that the patients in group 2 presented with a smaller diastolic right ventricle (31.4 mm±7 mm vs 40.2 mm±8 mm; *P*<.001) and less systolic pressure in the pulmonary artery (38.9 mm Hg±15 mm Hg vs 48.2 mm Hg±20 mmHg; *P*=.001). Figure 2

TABLE 1. **Comparison of patients with ASD who underwent surgery before the age of 25 years (group 1), after the age of 25 years (group 2), and adult patients with ASD who did not undergo surgery**

	Group 1 (n=102)	Group 2 (n=90)	Group 3 (n=88)
Mean age, years	22±7*	52±13	49±16
Female sex, %	62	68	67
Ostium primum type, %	34*	9	10
Pulmonary flow/systemic flow	–	2.9±0.9 (63)	2.6±0.8 (77)
Diameter of the defect mm	–	24±9 (61)	22±7 (75)
Postoperative follow-up, years	11±8*	6.6±6	–
Diastolic size of the RV, mm	24±8* (82)	31±7** (77)	40±8 (78)
Systolic pulmonary pressure, mm Hg	31±14* (89)	39±15**	(85) 48±20 (80)
Degree of mitral insufficiency, 0-3	1.0±0.9	0.9±0.9	0.8±0.8
Degree of tricuspid insufficiency, 0-3	1.0±0.6*	1.45±0.9	1.4±0.7
LV shortening fraction, %	34±4 (88)	35±6 (74)	35±8 (69)
Diameter of the left ventricle, mm	38±7* (98)	48±10 (88)	46±10 (83)
Atrial fibrillation, %	6*	27***	15

**P*<.001 with respect to group 2. ***P*<.001 with respect to group 3. ****P*=.51 with respect to group 3. The numbers in parenthesis indicate the number of cases on which each estimate is based; their absence indicates that the data was available for all cases. RV indicates right ventricle; LV, left ventricle.

TABLE 2. **Comparison of patients who underwent surgery for ostium primum, ostium secundum, or venous sinus ASD**

	Ostium primum (n=43)	*Ostium secundum or venous sinus* (n=149)	*P*
Age, years	28±12	38±19	<.001
Female sex, %	46.5	70	.008
Age at surgery, years	14±13	31±20	<.001
Post-operative follow-up, years	14±6	8±7	<.001
Diastolic RV size, mm	30±13 (35)	27±7 (124)	.28
Pulmonary systolic pressure, mm Hg	37±18 (41)	34±14 (133)	.42
Degree of mitral insufficiency (0-3)	1.9±0.6	0.7±0.8	<.001
Degree of tricuspid insufficiency, 0-3	1.4±0.7	1.2±0.8	.053
LF shortening fraction, %	34±5 (35)	35±5 (127)	.17
Left ventricle diameter, mm	44±9 (41)	42±11 (145)	0.32
Atrial fibrillation, %	12	17	.38

The numbers between parentheses indicate the number of cases on which each estimate is based; their absence indicates that the data was available for all cases. RV indicates right ventricle; LV, left ventricle.

TABLE 3. **Comparison between the patients in the 3 groups, excluding those patients with ostium primum ASD**

	Group 1 (n=67)	Group 2 (n=82)	Group 3 (n=79)
Mean age, years	21±7[a]	52±14	50±16
Female sex, %	70	69	71
Pulmonary flow/systemic flow	–	3.0±0.9 (60)	2.7±0.7 (71)
Diameter of the defect, mm	–	24±9 (59)	22±7 (68)
Postoperative follow-up, years	9±8[b]	6±6	–
Diastolic size of the RV, mm	22±5[a] (57)	31±7[d] (67)	40±7 (72)
Systolic pulmonary pressure, mm Hg	28±4[a] (56)	39±16[e] (77)	46±15 (72)
Degree of mitral insufficiency, 0-3	0.6±0.7[c]	0.8±0.9	0.7±0.7
Degree of tricuspid insufficiency, 0-3	0.9±0.6[a]	1.4±0.9	1.4±0.7
LV shortening fraction, %	34±4 (60)	36±6 (67)	35±8 (62)
Left ventricle diameter, mm	36±7[a] (64)	48±10 (81)	46±10 (76)
Atrial fibrillation, %	6[a]	26[f]	14

[a]*P*<.001 with respect to group 2 2. [b]*P*<.05 with respect to group 2. [c]*P*=.63 with respect to group 2. [d]*P*<0.001 with respect to group 3. [e]*P*<.01 with respect to group 3. [f]*P*=.64 with respect to group 3. The numbers in parenthesis indicate the number of cases on which each estimate is based; their absence indicates that the data was available for all cases. RV indicates right ventricle; LV, left ventricle.

shows that the degree of tricuspid insufficiency and dilatation of the left atrium were similar in patients who had undergone surgery and those who had not, and that the prevalence of atrial fibrillation was greater in the patients who had surgery. There were 24 patients (27%) in atrial fibrillation in group 2 and 13 in atrial fibrillation (15%) in group 3, although the difference was within the limits of statistical significance (*P*=.051).

DISCUSSION

The principal consequence of ASD is a volumetric overload of the small annula that causes progressive dilatation of the right ventricle and increases pulmonary pressure. These hemodynamic effects may be well-tolerated for decades, but eventually cause right ventricular dysfunction and cardiac insufficiency. Tricuspid valve insufficiency secondary to annular dilatation aggravates right failure. Dilatation of the right ventricle and abnormal movement of the septum changes left ventricle function. The left atrium dilates to a degree proportionate to the increase in pulmonary venous return, the changes in the diastolic function of the left ventricle, and the degree of mitral valve insufficiency. As a consequence, a great incidence of atrial arrhythmias is produced, as well as thromboembolic complications that aggravate the development of ASD in adults. When the ASD is closed before the age of 25 years, the majority of these changes normalize, but the hemodynamic and electrophysiological course of patients who undergo surgery in their adult years has not been well established.[8-13]

Pulmonary pressure and right ventricle size

Closure of an ASD surgically or by percutaneous procedure[20,21] overrides the short circuit from left to right and the volumetric overload of the right ventricle. Consequently, pulmonary pressure and the size of the right ventricle must be reduced.[22,23] This study confirms that systolic pulmonary pressure is lower and the size of the right ventricle smaller in patients who undergo surgery in comparison with adult patients who have not undergone surgery. But it also shows that pulmonary pressure and the size of the right ventricle are significantly greater in patients who undergo surgery after 25 years of age than for those who undergo surgery before the age of 25 years.

The relative increase in pulmonary pressure in patients who undergo surgery after 25 years of age implicates the presence of an increase in arteriolar pulmonary resistance that persists after surgery, whether it be an increase in passive resistance due to elevation of pressure in the left atrium and pulmonary capillary or a decrease in the elastic properties of the pulmonary arteries caused by chronic dilatation. In all likelihood the 3 mechanisms co-exist to a greater or lesser degree in different patients, contributing to the maintenance of an increase in the right ventricular afterload following the intervention.

Residual dilatation of the right ventricle in the absence of a volume overload also indicates an increase in afterload and a decrease in systolic function. The increased pulmonary pressure may contribute to the dilatation of the right ventricle, but probably the effect of the remodeled ventricle as a consequence of a long-standing volumetric overload plays a much more important role. In any case, persistent right ventricle dilatation causes geometric changes that tend to be progressive and can affect the competence of the tricuspid valve and interact with the function of the left ventricle.

Tricuspid insufficiency

The association between tricuspid valve insuffi-

ciency and ASD has been noted less frequently in the literature than mitral valve insufficiency,[24,25] but our study shows that tricuspid insufficiency is frequent in ASD in adults. Twenty-five (9%) of the 280 patients included in our series had serious tricuspid valve insufficiency (3 out of 3) The etiology of tricuspid insufficiency, like mitral valve insufficiency, may depend on anatomical changes or mixoid degeneration, but more likely is a result of hemodynamic changes in the right ventricle, annular dilatation, and mechanical dysfunction of the sub- valve apparatus.[10] This study shows that the degree of tricuspid insufficiency is greater in patients who undergo surgery during their adult life than those undergoing surgery before they are 25 years of age. Only 2 patients (2%) who had surgery before the age of 25 years presented with serious tricuspid valve insufficiency, in comparison with 16 (18%) of the patients who were operated on after the age of 25 years. Even more important is the finding that the degree of tricuspid insufficiency was similar among patients who underwent surgery after 25 years of age and those adult patients who did not undergo surgery.

Left ventricle

Although in some patients with serious right ventricle volume overload systolic function of the left ventricle became depressed,[26] previous studies have demonstrated that the majority of patients with ASD maintain normal systolic function of the left ventricle, in spite of presenting with symptoms of cardiac insufficiency.[27] In our study, we did not find significant differences in systolic function of the left ventricle, evaluated by shortening fraction, among the 3 groups analyzed. The use of the shortening fraction could be criticized in the presence of a volume overload of the right ventricle and a paradoxical movement of the septum. Nevertheless, after surgical intervention the movement of the septum normalized in the majority of cases, thus increasing the trustworthiness of this method. In any case, our study shows that the systolic function of the left ventricle remains normal in patients undergoing surgery early or later, and there was no significant difference between the 2 groups.

Dilatation of the right ventricle produces changes in cardiac architecture that affect ventricular interrelation. During diastole, the interventricular septum is displaced toward the left ventricle and the normal curvature of the septum flattens out or inverts itself, reaching maximum displacement and geometric distortion at the end of diastole. As a consequence, it produces a decrease in the diameter and diastolic volume of the left ventricle and of myocardial distensibility.[28,29] Long term, the decrease in distensibility of the left ventricle causes restriction upon filling and increases the telediastolic pressure. In patients who undergo surgery as adults who have residual dilatation of the right ventricle and permanent alteration of the diastolic pressure/volume ratio in this cavity, secondary changes are produced in the diastolic function of the left ventricle.[30] Nevertheless, in patients who undergo surgery in infancy or childhood persistent changes in left ventricular function have not been demonstrated.[8]

Mitral insufficiency

Mitral insufficiency is the cardiac damage most frequently associated with ASD of the *ostium primum*,[31,32] but it is also relatively frequent in ASD of the *ostium secundum* or venous sinus.[33,34] These mitral valve changes have been attributed to the abnormal geometry of the left ventricle in response to dilatation of the right ventricle. The incidence of these lesions increases with age[35] and can progress after surgery performed during adulthood.[36] In our series, there were 17 patients (5.6%) with grade 3 mitral insufficiency, but the degree of regurgitation was not significantly different among the 3 groups. Although patients with *ostium primum* ASD presented with a higher degree of mitral insufficiency, the exclusion of patients with *ostium primum* ASD from the analysis of data did not change the results. Nevertheless, there was a tendency to greater mitral regurgitation in those patients who underwent surgery after 25 years of age as compared to those operated on before the age of 25 years (P=.067).

Left atrium size

The increase in the size of the left atrium is a common finding in adult ASD, with or without surgical intervention. In our series, the size of the left ventricle was greater than 40 mm in 151 patients (54% of the total) and greater than 50 mm in 62 patients (22% of the total). Dilatation of the left atrium may be due to the increase in volume caused by the interatrial short-circuit, but may also be related to the degree of mitral valve insufficiency and the diastolic properties of the left ventricle.[28,29] In our study we did not evaluate the diastolic function of the left ventricle, but it is very significant that the size of the left atrium was much smaller in those patients who underwent surgery before the age of 25 years than in those who underwent surgery after the age of 25 and in those patients who did not undergo surgery, although there were no significant differences in the degree of mitral insufficiency. The contribution of volume overload to the increase in size of the left atrium does not appear to be important, as those patients who underwent closure of the ASD after the age of 25 years had the same or even greater left atrium size than the patients who did not undergo surgery. Indeed, in the patients who did not have previous surgery there was no relationship between the

amount of Qp/Qs and the size of the left atrium (r=0.11; *P*=.24).

Atrial fibrillation

Atrial fibrillation is a change in cardiac rhythm that results in a great increase in the mortality-morbidity rate in adult ASD.[37,38] This arrhythmia is much more frequent in patients who survive naturally into adulthood than patients who undergo surgery for ASD in childhood.[1,2] In patients who undergo surgery during adulthood, AF on many occasions persists or appears despite the intervention.[3-6,11] Our study shows that the prevalence of AF in adult patients who underwent surgery before the age of 25 years is low, and substantially inferior to that in patients who have undergone surgery after the age of 25 years and those who did not undergo surgery. On the other hand, the prevalence of AF was higher in patients who underwent surgery after the age of 25 years than in those who did not undergo surgery, although this difference was at the limit of statistical significance (*P*=.051).

The cause of AF in ASD has not been determined and is probably multifactorial in nature. It has been proposed that it is related to atrial dilatation, the increase in pulmonary pressure, and ventricular dysfunction. The stretching of the atrium wall prolongs the atrial refractory period heterogeneously, making the atrium more vulnerable to the induction of fibrillation.[39,40] The diastolic properties of both ventricles may also be involved in atrial arrythmogenesis. Gatzoulis et al[13] and Oliver et al[41,42] have shown that the risk of atrial arrhythmias after surgery is related to the patient´s age at the time of intervention. In the Gatzoulis series, all the patients who developed atrial arrhythmias were more than 40 years of age at the time of surgery, but these authors did not differentiate the effect of age *per se* from the age at the time of intervention. Recently, our group published results that indicate that age at the time of surgery is only an independent factor in the reduction of the risk of AF when surgery is performed before the age of 25 years.[41,42]

The greater prevalence of AF in patients who undergo surgery after the age of 25 years with respect to that in patients who have not undergone surgery may be related to the selection of patients for surgery, as supraventricular arrhythmias may be the first symptomatic manifestation of adult ASD. Nevertheless, we have shown previously that the principal factors related to the development of AF in adult ASD are advanced age, the size of the left atrium, and the degree of mitral and tricuspid insufficiency.[42] In our study, the age of patients who underwent surgery after the age of 25 years was slightly greater than that of patients who did not undergo surgery and presented with greater dilatation of the left atrium and greater degree of mitral or tricuspid insufficiency. Although none of these differences was statistically significant, the conjunction of the 4 independent risk factors may justify the greater prevalence of AF in patients who undergo surgery after the age of 25 years than in patients over the age of 25 years who have not undergone surgery. Another factor that may be involved in the greater prevalence of AF in patients who have undergone surgery is the development of re-entrance macro circuits around the atriotomy scar.[43] Nevertheless, «incisional» arrhythmias tend to correspond to interatrial tachycardia or uncommon atrial flutter rather than AF.[44] On the other hand, scar arrhythmias do not justify the greater prevalence of AF in patients who underwent surgery after the age of 25 years in comparison with those who underwent surgery before the age of 25 years.

Limitations

This is a retrospective study and therefore has the limitations inherent in this type of analysis. A long-term prospective study to evaluate the differences between early surgical intervention and the natural course of the disease does not appear feasible. By being an observational study, with groups of patients of very different ages, it is possible that the profile of the patients in each group may be different. In fact, in group 1 there was a greater percentage of patients with *ostium primum* ASD, but this would reinforce rather than invalidate the results, as the patients who underwent surgery before the age of 25 years had a better disease course in spite of the fact that more patients with *ostium primum* ASD were included, who theoretically could have more serious postoperative residua. The most confusing factor in the analysis of the data was the difference in age between groups 1 and 2. In our study we showed that age is a predisposing factor for AF, independently of whether the ASD had been closed or not,[42] and the same may occur with the hemodynamic changes analyzed. Echocardiography and cardiac Doppler studies were well validated by the evaluation of the size of the cavities, left ventricular function, degree of valve insufficiency, and systolic pulmonary pressure, but not all the parameters analyzed could be obtained in all patients due to a bad acoustic window or other causes. In any case, the percentage of patients in whom 1 of the variables analyzed was lacking was small and should not affect the mean values. The possible limitations of using the shortening fraction as an index of left ventricular function has been commented on previously, and this was the only index available in our database. The prevalence of atrial arrhythmias would have been greater if repeated Holter studies had been performed, but only a limited number of patients had Holter studies available for analysis. The greater uncertainty may be with regard to the selection of the group with natural evolu-

tion of the disease. These patients were adults of more than 25 years of age with non-restrictive ASD (defect size>15 mm and Qp/Qs>1.5) who had not undergone surgery at the time of our study. The majority of these patients later underwent surgery, but the indication for surgery was established by their referring physicians independently of the results of our study, and a clinical evaluation and complete echocardiography study performed a year after the intervention was not available to us. In any case, this group of patients is not differentiated from the group who underwent surgery after the age of 25 years with regard to the anatomical type of ASD, age, sex, size of the defect, or Qp/Qs, so that it could be considered a good control group.

Therapeutic implications

Our study shows that the hemodynamic and electrophysiological results of the surgical repair of ASD after the age of 25 years are significantly inferior to those obtained when surgery is performed before this age. The reduction of pulmonary pressure and the size of the right ventricle are significantly less in those patients who underwent surgery after the age of 25 years and, while the degree of tricuspid insufficiency was significantly reduced in those patients who underwent surgery before the age of 25 years, as was the size of the left ventricle and the prevalence of chronic atrial fibrillation, surgery performed after the age of 25 years did not result in a reduction in these changes. These findings indicate that we should concentrate our efforts on trying to close all hemodynamically significant ASDs during childhood and in any case before the age of 25 years, in order to avoid during adulthood the undesirable clinical consequences of persistent hemodynamic and electrophysiological changes.

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